REMARKS

In response to the appeal brief of June 30, 2008, the Office reopened prosecution setting forth new grounds of rejections in the Office Action of October 3, 2008. This is a reply to this Office Action under 37 CFR §1.111.

Claims 48 to 81 are pending in this application. Claim 69 is withdrawn. Claims 77 to 81 are new. Claims 48, 57 and 66 are in independent form.

On page 3, the Office rejected claims 48-55, 57-62, 64-67 under 35 USC 102(b) as being anticipated by Stagljar et al. (PNAS 95:5187-5192, 1998, specifically pp. 5187, 5191 and figure 2; hereinafter "Stagljar").

Applicants previously argued that the bait and prey vectors are maintained episomally and that in contrast, Stagljar's bait vector is integrated into the yeast genome.

While acknowledging that Stagljar's bait vector indeed integrates, the Office's new anticipation rejection is based on the definition of the Merriam-Webster dictionary, which was said to define the term "episomal" as:

> "a genetic determinant (as the DNA of some bacteriophages) that can replicate autonomously in bacterial cytoplasm or as an intergral part of the chromosomes."

The Office expressed the opinion that the above definition constitutes the "broadest reasonable interpretation" consistent with the specification of the term "episomal".

Applicants note that the above definition is in fact for the noun "episome." The adjective and the adverb are not separately defined.

During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." While the MPEP alerts the reader to the fact that it is improper to import into a claim limitations that are not part of the claim (MPEP §2111.01), the claim are to be interpreted not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367

F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). (MPEP § 2111).

The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999) (The Board's construction of the claim limitation "restore hair growth" as requiring the hair to be returned to its original state was held to be an incorrect interpretation of the limitation. The court held that, consistent with applicant's disclosure and the disclosure of three patents from analogous arts using the same phrase to require only some increase in hair growth, one of ordinary skill would construe "restore hair growth" to mean that the claimed method increases the amount of hair grown on the scalp, but does not necessarily produce a full head of hair.).

The court in *In re Cortright* noted that the "PTO's interpretation of claim terms should not be so broad that it conflicts with the meaning given to identical terms in other patents from analogous art." Id. at 1359.

Applicants will show below that the term "maintained episomally" is consistently used as the opposite of "integrated" in patents covering analogous art including in patents recently issued in the USPTO art unit in which the present application is examined.

U.S. Patent **7,435,546**, issued on October 14, 2008 and was examined not only in the same Art Unit (1636) but also by the same Examiner as the present application.

For example, claim 2 of this patent recites "the first reporter gene and transcriptional regulatory sequence are integrated into the a chromosome . . . or maintained episomally." The specification does not define the term "episomally", but states, among others that "since such a plasmid is maintained episomally in a circular form, it can be readily introduced and recovered from a bacterial host."

U.S. Patent **7,446,188**, issued on August 14, 2008 and was examined in Art Unit 1638.

The specification uses the term "episomally" as follows: "The gene can be maintained episomally or the gene can be integrated into the chromosome."

U.S. Patent **6,642,051**, issued on November 3, 2003 and was examined in the Art Unit of the present application.

The abstract notes that "constructs may be either integrated into a mammalian cell genome or maintained episomally."

Other patents of interest, all of which use the term "maintained episomally" in the claims are in particular, US Patent 6,902,882 (Art Unit: 1632), 6,015,669 (Art Unit: 1655) and 5,876,931 (Art Unit: 1636).

Nonethelss, to further the prosecution of this case, applicants have amended the claims to clarify that the bait and prey vectors are "plasmid constructs." The amendment is supported by the description of the "bait vector" starting on [0086] of the specification as published (see in particular page 22, line 20 of the specification as filed) and the description of the "prey vector" starting on [0122] of the specification as published (see in particular page 37, line 3 of the specification as filed). The Office is referred to the consistent use of the term "the plasmids" in the respective following paragraphs when referring back to the plasmid constructs (e.g., page 22, line 27, page 23, lines 1, 5 etc. and page 37, lines 6, 12, 16, 20 etc.).

A plasmid is, according to the Merriam-Webster online Dictionary used by the Office, "an extrachromosomal ring of DNA especially of bacteria that replicates autonomously."

The amended claim language thus provides for episomally maintained plasmid constructs, a term which amply clarifies that the bait and prey vector are not integrated. See also US Patent 7,390,636 (Art Unit :1636) of June 24, 2008.

The Office is also referred to new claims 78 to 81, which recite propagation via a CEN/ARS and 2microns origin of replication, ergo, extrachromosomal propagation. The amendments are supported by, e.g., the paragraph starting on line 5 of page 23 and on line 20 of page 38, respectively.

Considering these explanations and amendments, applicants respectfully refer the Office to applicants reasoning presented in the appeal brief of June 30, 2008 which is incorporated herein in its entirety.

Here, appellant argued:

Stagljar does not disclose anywhere that both the Nub and the Cub-PLV (PLV = transcription factor) plasmids are maintained episomally. Moreover, the Cub containing plasmid pRS305 (Δwbp1-Cub-PLV) does not contain the entire the entire WBP1 open

reading frame. Rather the plasmid contains a 5'-truncated "Δwbp1 gene" (see page 5188, left col., l. 15) and, to put it in Stagljar's words, the WBP1-Cub-PLV fusion gene is "generated by site-directed integration of a 5'-truncated Δwbp1 gene (Δwbp1-Cub-PLV) into the genomic WBP1 locus." (see page 5189, left col., l. 7 to l. 10). Thus, the yeast genome provides, upon integration, next to the Wbp1 promoter to drive expression (see description of pRS305 on page 5188, left col. starting on page 14), the N-terminal part of the Wbp1 ORF to provide a full Wbp1-Cub-PLV fusion protein. Stagljar then tests this full Wbp1-Cub-PLV fusion protein for interaction with Ost1-Nub and Nub-Alg5p (see page 5189, right col., starting on l. 6).

With regard to claims 66 and 67, applicants note that there is no promoter in pRS305 (see weblink cited by the Office) that is part of an expression cassette as set forth in claim 66. The Office is referred to elements (i) to (v) of this expression cassette. The promoters present in pRS305 are (1) the *E. coli* promoter driving expression of the lac gene for selection on ampicillin containing medium in *E. coli*, (2) T7 and T3 promoters for (a) bacterial expression or (b) expression in cell-free extracts supplemented with T7 polymerase. These promoters are not part of an expression cassette having the elements recited in claim 66.

On pages 4 and 5, the Office rejected claims 68 and 70 under 35 USC §103(a) as being unpatentable over Stagljar as applied to claims 48-55, 57-62, and 64-67 and further in view of Ehrhard et al.

The Office argued Stagljar anticipated the kit of claims 57 to 65, but did not teach a method of identifying pharmaceutical drugs for their ability to interfere with protein-protein interactions. Ehrhard et al is said to teach a method of identifying compounds for their ability to interfere with protein-protein interactions.

Stagljar does not anticipate the kit claims for the reasons set forth above. There is no explanation provided how the deficiencies of Stagljar are cured by Ehrhard et al. and applicants submit that these deficiencies are indeed not cured by Ehrhard et al. Accordingly, no *prima facie* case of obviousness has been established.

On page 5, the Examiner rejects claim 56 under 35 USC §103(a) as being unpatentable over

Stagljar et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Wedegaertner et al (hereinafter "Wedegaertner").
The Office acknowledges that Stagljar does not teach the protein attached artificially to the membrane.
Wedegaertner is said to disclose lipid modification of G proteins so that they attach to the membrane. Motivation to combine the two teachings is said to flow from the fact that Wedegaertner teaches that that fatty acylation regulates cellular localization.

Unaddressed deficiencies of Stagljar in addition to those noted by the Office have been discussed above.

For the sole purpose of furthering the prosecution of this case, applicants have further specified the type of fusion as one to a signal sequence which encodes a membrane anchor. Support for this amendment can be found in paragraph [0149] of the present publication (page 43, lines 25 and 26 of the specification as filed).

On page 6, the Office rejected claims 63, 75, and 76 under USC §103(a) as being unpatentable over Stagljar as applied to claims 48-55, 57-62, 64-67 above, and further in view of Ecker et al (hereinafter "Ecker").

The Office acknowledges that Stagljar does not teach a CUP1 promoter in the bait vector. Ecker is said to teach the use of the CUP1 promoter for expression of the ubiquitin gene in yeast.

Unaddressed deficiencies of Stagljar in addition to those noted by the Office have been discussed above.

While, Stagljar has been discussed in detail before, briefly, Stagjlar describes a genetic system based on the detectable reconstitution of native ubiquitin from fragments.

Ecker discloses the synthesis and expression of a cassette adapted ubiquitin gene to study the characteristics and functions of the gene. The gene contains restriction enzyme sites to facilitate studies involving site directed mutagenesis. The gene was expressed under the CUP1 promoter which resulted in high levels of ubiquitin accumulation. Certain features of

the CUP1 promoter are discussed.

Relying on a motivation to combine rationale, the Office describes as the motivation to combine the two teachings the fact that Ecker teaches that the CUP1 promoter can be partially repressed, which would lead to lower levels of expression. The Office does not provide any rationale why the person skilled in the art would find it desirable to provide such a promoter in the context of Stagljar's system. Instead the Office cites pages of Ecker noting conflicting findings with respect to CUP1 promoter regulation, which by itself rather provides a disincentive than an incentive to use this promoter (See MPEP 2141.01 III stating "the mere fact that references can be combined or modified does not render the resultant combination obvious unless **>the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)").

Thus, no *prima facie* case of obviousness has been established by the Office.

However, for the sole purpose of furthering the prosecution of this case, applicants have amended claim 76 to remove the reference to a CUP1 promoter (please note new claim 76, which finds support in claim 76).

On page 7, the Office rejected claims 71-73 under USC §103(a) as being unpatentable over Stagljar as applied to claims 48-55, 57-62, 64-67 above, and further in view of Clarke et al. (hereinafter "Clarke").

The Office acknowledged that Stagljar, while teaching the use of a CEN/ARS origin of replication in the Nubl-ALG5 vector, do not teach the use of a CEN/ARS origin of replication in the bait vector.
Clarke is said to teach the use of the CEN/ARS vector as a low copy vector.
Relying on a motivation to combine rationale, the Office describes as the motivation to combine the two teachings the fact that Clarke teach that the CEN/ARS vector is only 1-2 copies per cell. The Office does not provide any rationale why the person skilled in the art would find it desirable to provide such a CEN/ARS origin of replication in the context of Stagljar's system.
Stagljar, as the Office noted, being fully aware of the existence of CEN/ARS vectors and their origins of replication, did rather use an integrating vector.

Clarke discusses the use of extrachromosomal replication elements for use in expression vectors.

Clarke notably states on page 32 (specifically referenced by the Office), at the end of the second full paragraph "nevertheless, *CEN/ARS* plasmids are two to three orders of magnitude less stable than normal yeast chromosomes (see below)". (*emphasis added*)

Thus, considering that Stagljar advocates for and uses an integrated bait vector and Clarke states that they are less stable than normal yeast chromosomes, there seems be no motivation for a person skilled in the art to use a CEN/ARS based bait vector in Stagljar's system (see MPEP §2143 (G) for current requirements for the obviousness rationale used by the Office).

Accordingly, applicants respectfully submit that Office has not established a *prima facie* case of obviousness.

Applicants, having shown that all claims as currently presented are neither anticipated nor made obvious by the art applied, respectfully request an early allowance of this case.

The Commissioner is authorized to charge any fee deficiencies or overpayments to undersign's deposit account 50-3135.

Respectfully submitted,

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